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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,474	07/14/2004	Stephen Neidle	1090-102	2378

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EXAMINER	
RAHMANI, NILOOFAR	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 09/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/501,474	NEIDLE ET AL.	
	Examiner	Art Unit	
	Niloofar Rahmani	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *78-140* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *78,110-113 and 136-140* is/are rejected.

7)☒ Claim(s) *79-109,114-135* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 78-140 are pending and claims 1-77 are cancelled in the instant application.

2. ***Priority***

This application is a 371 of PCT/GB03/00102, filed on 01/14/2003, which claims the priority of UNILTED STATES OF AMERICA 60347899, filed on 01/15/2002.

3. The rejection of claims 87, 114-118, 120, 122-123 for "NR^1R^2, NR3R4" under 112, second paragraph is withdrawn in view of applicants amendment.

4. The rejection of claims 134-135 for "RN" under 112, second paragraph is withdrawn in view of applicant's amendment.

5. The rejection of claims 78,80,82,84-86,88,112,130,132-133 under 102(b) over Gamage et al. is withdrawn in view of applicant's amendment and argument.

6. The rejection of claims 78,79,82,84-86,88,130,132,133 under 103(a) over Read et al. and Gamage et al. is withdrawn in view of applicant's amendment and argument.

7. The rejection of claims 78, 136 for "hydrates" under 112, first paragraph and second paragraph is maintained for reason of record. Applicants argue that one ordinary skill will appreciate that the hydrates of the claims includes all possible hydrates and is therefore clear. It is the examiner's position that hydrate is unpredictable because there are different hydrates. There are ½ hydrate, 3

hydrates, or ¾ hydrate, etc. therefore, the specification lacks description of "hydrates".

8. The rejection of claim 137 for " therapeutically effective amount" under 35 U.S.C. 112, second paragraph is maintained for reason of record. Applicants have not argued for claiming "pharmaceutical composition". It is the examiner's position that pharmaceutical composition by definition must be effective yet non-toxic. Claim 137 is pharmaceutical composition without dosage limitation i.e. included both ineffective and toxic amount. It is recommended that "therapeutically effective amount" be incorporated in the claim.

9. The rejection of claims 110-113 for "t" under 112, second paragraph is maintained for reason of record. Applicants argue that the claims are amended to obviate the rejection. It is the examiner's position that the term "t" is unclear. The definition of "t" is vague and unclear. One claim defines t being 0-3, the other defines t being 0-4 or 0-5. If "t" has different value, then the applicants need to define different t such as t', t'', t''', etc. correction is required.

10. The rejection of claims 110-113 for " R" under 112, second paragraph is maintained for reason of record. Applicants argue that the claims are amended to obviate the rejection. It is the examiner's position that the term "R" is unclear. The definition of "R" is vague and unclear. R defined in the claims as being independently a substituent, which can be anything. Correction is required.

11. The rejection of claims 138-140 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for reason

of record. Applicants argue that to submit that demonstration of clinical efficacy is not a requirement of the Patent Law. Moreover, the Examiner is requested to see the attached Johnson et al. (British Journal of Cancer (2001) 84(10), 1424-1431), which demonstrates that clinical efficacy can be predicted based on in vitro tests. Specifically, the attached reference demonstrates a correlation between positive results in *in vitro* models and clinical trials *in vivo*. Further, the examiner is requested to see the applicants copending U.S. Patent Application # US 2003-0207909, which demonstrates that inhibition of telomerase *in vitro* relates to activity *in vivo* for treating cancer. It is the examiner's position that applicant has not shown the nexus for inhibition telomerase in vitro or in vivo and treating or preventing any and all known diseases. Johnson et al. tested in pre-clinical *in vivo* and *in vitro* assays by the National Cancer Institute's Developmental Therapeutics Program. "For 39 agents with both xenograft data and Phase II clinical trials results available, in vivo activity in a particular histology in a tumor model did not closely correlate with activity in the same human cancer histology, casting doubt on the correspondence of the pre-clinical models to clinical results." Application # 2003-0207909 has nexus between compounds and Cytotoxicity activity of the correlated compounds on Table I, page 64. No information was found in the specification that associated using the claimed compounds with the treatment any cancer in the Application # 2003-0207909.

12. The rejection of claims 138-140 " method of inhibiting telomerase, regulating or treatment of cell proliferation in vitro or in vivo, comprising

contacting a cell with an effective amount of a compound according to claim 78" under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained for reason of record. Applicants argue that the attached Johnson et al. demonstrates that clinical efficacy can be predicted based on *in vitro* tests. Moreover, the attached copending U.S. Patent application provides evidence that inhibition of telomerase *in vitro* relates to activity *in vivo* for treating cancer. The level of skill in the art is advanced and no more than reasonable experimentation would be required to make and use the invention of the rejected claims. It is the examiner's position that applicant has not shown the nexus for inhibition telomerase in vitro or in vivo and treating or preventing any and all known diseases. Johnson et al. tested in pre-clinical *in vivo* and *in vitro* assays by the National Cancer Institute's Developmental Therapeutics Program. "For 39 agents with both xenograft data and Phase II clinical trials results available, in vivo activity in a particular histology in a tumor model did not closely correlate with activity in the same human cancer histology, casting doubt on the correspondence of the pre-clinical models to clinical results." Application # 2003-0207909 has nexus between compounds and Cytotoxicity activity of the correlated compounds on Table I, page 64. No information was found in the specification that associated using the claimed compounds with the treatment any cancer in the Application # 2003-0207909. In the instant case, the instantly claimed invention is highly unpredictable since the applicants need to test the compounds in vivo. Those of skill in the art recognize that in vitro assays and or

cell-cultured based assays are generally useful to observe basic physiological and cellular phenomenon such as screening the effects of potential drugs. However, clinical correlations are generally lacking. The greatly increased complexity of the in vivo environment as compared to the very narrowly defined and controlled conditions of an in- vitro assay does not permit a single extrapolation of in vitro assays to human diagnostic efficacy with any reasonable degree of predictability. In vitro assays cannot easily assess cell-cell interactions that may be important in a particular pathological state. Furthermore it is well known in the art that cultured cells, over a period time, lose phenotypic characteristics associated with their normal counterpart cell type. Freshney (Culture of Animal Cells, A Manual of Basic Technique, Alan R. Liss, Inc., 1983, New York, p4) teach that it is recognized in the art that there are many differences between cultured cells and their counterparts *in vivo*. These differences stem from the dissociation of cells from a three-dimensional geometry and their propagation on a two-dimensional substrate. Specific cell interactions characteristic of histology of the tissue are lost. The culture environment lacks the input of the nervous and endocrine systems involved in homeostatic regulation *in vivo*. Without this control, cellular metabolism may be more constant *in vitro* but may not be truly representative of the tissue from which the cells were derived. This has often led to tissue culture being regarded in a rather skeptical light (p. 4, see Major Differences *In Vitro*).

13. ***Claim Objections***

Claims 79-109, 114-135 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Niloofar Rahmani whose telephone number is 571-272-4329. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas Mckenzie, can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

NILOOFAR RAHMANI
09/08 /2006
NR

D.MARGARET SEAMAN
PRIMARY EXAMINER
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